

1. An isolated human *FOXC2* promoter region comprising a nucleotide sequence selected from the group consisting of:

(a) nucleotides 1692 to 1703 of SEQ ID NO:1, or a fragment thereof exhibiting *FOXC2* promoter activity;

5 (b) a sequence complementary to (a); and

(c) the sequence of a nucleic acid capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence as defined in (a) or (b).

2. The human *FOXC2* promoter region of claim 1, comprising a nucleotide sequence selected from the group consisting of:

(a) nucleotides 1250 to 1749 of SEQ ID NO:1, or a fragment thereof exhibiting *FOXC2* promoter activity;

(b) a sequence complementary to (a); and

15 (c) the sequence of a nucleic acid capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence as defined in (a) or (b).

3. The human *FOXC2* promoter region of claim 2, comprising a nucleotide sequence selected from the group consisting of:

20 (a) nucleotides 1250 to 2235 of SEQ ID NO:1, or a fragment thereof exhibiting *FOXC2* promoter activity;

(b) a sequence complementary to (a); and

(c) the sequence of a nucleic acid capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence as defined in (a) or (b).

25 4. A recombinant construct comprising the human *FOXC2* promoter region of claim 1.

5. The recombinant construct of claim 4, wherein the human *FOXC2* promoter region is operably linked to a nucleic acid molecule comprising a nucleotide sequence that encodes a detectable product.

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6. The recombinant construct of claim 5, wherein the detectable product is a *FOXC2* polypeptide.

7. The recombinant construct of claim 4, further comprising a reporter gene.

8. A vector comprising the recombinant construct of claim 4.

9. A host cell stably transformed with the recombinant construct of claim 4.

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10. A method for identification of an agent regulating *FOXC2* promoter activity, the method comprising:

- (i) contacting a candidate agent with the human *FOXC2* promoter region of claim 1; and
- (ii) determining whether the candidate agent modulates *FOXC2* promoter activity.

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11. A method for identification of an agent that regulates *FOXC2* promoter activity, the method comprising assaying reporter gene expression in the presence of a candidate agent in a cell stably transformed with the recombinant construct of claim 7, wherein an effect on the level of expression of the reporter gene in the presence of the candidate agent as compared to the level of expression of the reporter gene in the absence of the candidate agent indicates that the agent regulates *FOXC2* promoter activity.

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12. An isolated human *FOXC2* enhancer region comprising a nucleotide sequence selected from the group consisting of:

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- (a) nucleotides 223 to 231 of SEQ ID NO:1, or a fragment thereof exhibiting *FOXC2* enhancer activity;
- (b) a sequence complementary to (a); and
- (c) the sequence of a nucleic acid capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence as defined in (a) or (b).

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13. An isolated human *FOXC2* enhancer region comprising a nucleotide sequence selected from the group consisting of:

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- (a) nucleotides 359 to 375 of SEQ ID NO:1, or a fragment thereof exhibiting *FOXC2* enhancer activity;
- (b) a sequence complementary to (a); and
- (c) the sequence of a nucleic acid capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence as defined in (a) or (b).

14. An isolated human *FOXC2* enhancer region comprising a nucleotide sequence selected from the group consisting of:

(a) nucleotides 378 to 402 of SEQ ID NO:1, or a fragment thereof exhibiting *FOXC2* enhancer activity;

5 (b) a sequence complementary to (a); and

(c) the sequence of a nucleic acid capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence as defined in (a) or (b).

10 15. An isolated human *FOXC2* enhancer region comprising a nucleotide sequence selected from the group consisting of:

(a) nucleotides 403 to 423 in SEQ ID NO: 1, or a fragment thereof exhibiting *FOXC2* enhancer activity;

(b) a sequence complementary to (a); and

15 (c) the sequence of a nucleic acid capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence as defined in (a) or (b).

16. The human *FOXC2* enhancer region of claim 12, comprising a nucleotide sequence selected from the group consisting of:

20 (a) nucleotides 216 to 475 of SEQ ID NO:1, or a fragment thereof exhibiting *FOXC2* enhancer activity;

(b) a sequence complementary to (a); and

(c) the sequence of a nucleic acid capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence as defined in (a) or (b).

25 17. A recombinant construct comprising a human *FOXC2* enhancer region of claim 12.

18. A vector comprising the recombinant construct of claim 17.

19. A host cell stably transformed with the recombinant construct of claim 18.

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20. A method for identification of an agent that regulates *FOXC2* enhancer activity, the method comprising:

contacting a candidate agent with the human *FOXC2* enhancer region of claim 12; and determining whether the candidate agent modulates *FOXC2* enhancer activity.

21. A method for identification of an agent that regulates *FOXC2* enhancer activity, the method comprising assaying reporter gene expression in the presence of a candidate agent in a cell stably transformed with the recombinant construct of claim 17, wherein an effect on the level of expression of the reporter gene in the presence of the candidate agent as compared to the level of expression of the reporter gene in the absence of the candidate agent indicates that the agent regulates *FOXC2* enhancer activity.

22. A method for identification of an agent that regulates a mammalian *FOXC2* promoter activity, the method comprising:

contacting an isolated nucleic acid sequence with a candidate agent, wherein the nucleic acid sequence comprises a murine *FoxC2* promoter nucleotide sequence shown as positions 1250 to 2235 in SEQ ID NO:5; and

determining whether the candidate agent modulates expression of a nucleotide sequence operably linked to the murine *FoxC2* promoter nucleotide sequence, such modulation indicating that the agent regulates mammalian *FOXC2* promoter activity.

23. A method for identification of an agent that regulates a mammalian *FOXC2* enhancer activity, the method comprising:

contacting an isolated nucleic acid sequence with a candidate agent, wherein the nucleic acid sequence comprises a murine *FoxC2* enhancer nucleotide sequence shown as positions 216 to 475 in SEQ ID NO:5; and

determining whether the candidate agent modulates expression of a nucleotide sequence operably linked to the murine *FoxC2* enhancer nucleotide sequence, such modulation indicating that the agent regulates mammalian *FOXC2* enhancer activity.

24. A method for identification of an agent that regulates a mammalian *FOXC2* enhancer activity, the method comprising:

contacting an isolated nucleic acid sequence with a candidate agent, wherein the nucleic acid sequence comprises a murine *FoxC2* enhancer nucleotide sequence shown as positions 216 to 2235 in SEQ ID NO:5; and

determining whether the candidate agent modulates expression of a nucleotide sequence operably linked to the murine *FoxC2* enhancer nucleotide sequence, such modulation indicating that the agent regulates mammalian *FOXC2* enhancer activity.

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25. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) SEQ ID NO:3 or a complement thereof;

5 (b) the sequence of a nucleic acid capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence complementary to the polypeptide coding region of a nucleic acid molecule as defined in (a) and which codes for a variant form of the FOXC2 transcription factor;

(c) the sequence of a nucleic acid which is degenerate as a result of the genetic code to a
10 nucleotide sequence as defined in (a) or (b) and which codes for a variant form of the FOXC2 transcription factor; and

(d) a nucleic acid that encodes the polypeptide of SEQ ID NO:4.

26. An isolated polypeptide comprising a polypeptide sequence encoded by the nucleic
15 acid molecule of claim 25.

27. The isolated polypeptide of claim 26, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:4.

20 28. A vector comprising the nucleic acid molecule of claim 25.

29. A replicable expression vector, that carries and is capable of mediating expression of the nucleotide sequence of claim 25.

25 30. A cultured host cell comprising the vector of claim 28.

31. A process for the production of a variant form of the FOXC2 transcription factor polypeptide, the process comprising culturing the host cell of claim 30 under conditions whereby the polypeptide is produced, and recovering the polypeptide.

30 32. A method for identifying an agent that regulates expression of the nucleic acid molecule of claim 25, said method comprising:

contacting a candidate agent with the nucleic acid molecule; and

FOXC2-09260-582E9660

D E S I G N A T I O N

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FOXC2 nucleotide sequence, comprising:

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(b) transfecting the cell line with a plurality of human cDNA sequences;

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(d) recovering cDNA from the isolated cells isolated in step (c); and

(e) identifying the polypeptide encoded by the cDNA recovered in step (d).

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